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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/251,073	02/16/1999	ROY R. LOBB	10274-003003	2802

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EXAMINER	
GAMBEL, PHILLIP	21

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/251073	Applicant(s) LOBB
	Examiner GAMBEL	Art Unit 1644

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 2/3/03

2a)☑ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-3, 6, 7, 9-13, 17, 18, 26-37

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 1-3, 6, 7, 9-13, 17, 18, 26-37

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☑ The drawing(s) filed on 2/3/03 is/are: a)☑ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☑ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

PAPER NO 21

DETAILED ACTION

1. Applicant's amendment, filed 2/3/03 (Paper No. 19), has been entered.
Claims 1, 12, 13 and 26 have been amended.

Claims 1-3, 6, 7, 9-13, 17, 18 and 26-37 are pending and under consideration.

Claims 4, 5, 8, 14-16 and 19-25 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 2/3/03 (Paper No. 19).
The rejections of record can be found in the previous Office Action (Paper No. 16).

3. Applicant has amended the first line of the specification to update the status of the priority documents, including USSN 08/822,830 and 08/456,193.

Again, as pointed out in the previous Office Action (Paper No. 16); given the priority issues concerning the instant claims as set forth previously and reiterated herein, applicant is invited to reconsider the priority claimed on the first line of the specification

The filing date of the instant claims is deemed to be the filing date of the priority application USSN 08/456,193, filed 5/31/95, as the previous priority applications do not provide sufficient written description for treating asthma with fibronectin and fibronectin-derived peptides encompassing the claimed limitations of the instant application.

If applicant desires priority prior to 5/31/95; applicant is invited to point out and provide documentary support for the priority of the instant claims. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

4. Formal drawings, filed 2/3/03 (Paper No. 20), have been submitted which comply with 37 CFR 1.84.

5. Applicant's amended claims to allergic asthma, filed 2/3/03 (Paper No. 19), have obviated the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Wayner et al. (U.S. Patent No. 5,730,978) .

6. Applicant's amended claims to allergic asthma, filed 2/3/03 (Paper No. 19) have obviated the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Kogan et al. (U.S. Patent No. 5,510,332).

7. Applicant's amended claims to allergic asthma, filed 2/3/03 (Paper No. 19) have obviated the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Arrhenius et al. (U.S. Patent No. 6,117,840).

8. Claims 1-3, 6, 7, 9-13, 17, 18 and 26-37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Wayner et al. (U.S. Patent No. 5,730,978) AND/OR Kogan et al. (U.S. Patent No. 5,510,332) AND/OR Arrhenius et al. (U.S. Patent No. 6,117,840) in view of art known of the nature and treatment of asthma at the time the invention was made as acknowledged in the Background of the Invention on pages 1-3 of the instant specification and pages 7-8 of the instant specification essentially for the reasons of record set forth in the previous Office Action (Paper No. 16).

Applicant's arguments, filed 2/3/03 (Paper No. 19), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant asserts that the prior art does not teach patients suffering from allergic asthma.

However, applicant also acknowledges that the general term asthma encompasses at least two different asthmatic disorders, namely allergic asthma, as claimed and non-allergic asthma. At the time of the priority date of the application, these two forms were known to exist as clinically distinct disorders having different incidences, etiologies and prognosis, as evidenced by the submissions from Dorland's Illustrated Medical Dictionary (1988) and the Merck Manual of Diagnosis and Therapy (1987). The skilled person would understand the term "asthma" used in Wayner refers to a genus of related but distinct disorders.

Therefore, in contrast to applicant's assertions and consistent with the prior art teachings as well as applicant's submissions for Dorland's Illustrated Medical Dictionary (1988) and the Merck Manual of Diagnosis and Therapy (1987) that the ordinary artisan would have immediately envisaged the treatment of allergic asthma, given the teaching of the treatment of asthma.

Also, as pointed out previously, the Background of the Invention (pages 1-3 of the instant specification) discloses the art known natural history of asthma, including the role of allergens in airway inflammation as well as early and late phase responses in allergen-induced asthma, wherein such patients are considered hypersensitive and discloses the art known of drugs to treat asthma by blocking or neutralizing the effects of inflammatory mediators before, during and after these responses.

Given the well known prevalence of the exposure of allergens leading to asthma and given the relatively small and known genus of asthmatic disorders, including the prior art teachings; the ordinary artisan would have treated or targeted allergic asthma with fibronectin polypeptides at the time the invention was made.

As pointed out previously, Wayner et al. teach methods of suppressing the immune response in human patients, including chronic and relapsing inflammation, including asthma by interfering the binding of receptor-ligand interactions between lymphocytes and endothelial cells (see Utility of the Invention, columns 15-17, including column 16, paragraph 1). Here, the inhibitory peptides may be administered by any route, including intravenously, intranasal and oral (column 16, paragraph 2 - column 17, paragraph 1). Wayner et al. teach that the inhibitory peptide comprising fibronectin, a portion of fibronectin including the fibronectin alternatively spliced IIICS region including the CS-1 domain comprising the EILDV motif which block adhesive events, including those with $\alpha 4\beta 1$ expressing lymphocytes and endothelial cells (see entire document, including Fibronectin, columns 3-7; Summary of the Invention, column 7-8; Detailed Description of the Invention, including columns 10 - 17 and Examples.

In addition to the teachings of treating asthma, Wayner et al. also teach treating allergy as well as asthma (e.g., see Summary of the Invention, including column 7, paragraph 2 and Utility of the Invention, including column 16, paragraph 1).

As pointed out previously, Kogan et al. teach methods of treating diseases associated with uncontrolled migration of white blood cells to damaged tissues such as asthma by inhibiting the binding of $\alpha 4\beta 1$ to VCAM-1 and that means for determining effecting inhibiting amounts are well known in the art (see Process of Inhibiting the Binding of $\alpha 4\beta 1$ Integrin to VCAM-1, columns 9-10). Here, the pharmaceutical compositions can be administered to humans by intravenous injection of intranasally via a spray or aerosol (see Pharmaceutical Composition; columns 8-9). Kogan et al. teach that $\alpha 4\beta 1$ recognizes fibronectin, including fibronectin isoforms including the CS1 peptide present in the alternatively spliced type III connecting segments (see Detailed Description of the Invention, including The Invention on column 3 and Peptides on columns 3-8 and Examples, including SEQ ID NO: 101)

In addition to the teachings of treating asthma, Kogan et al. also teach treating allergy as well as asthma (e.g. see columns 9-10, overlapping paragraph).

As pointed out previously, Arrhenius et al. teach methods of blocking interactions between the fibronectin peptide CS-1 and VLA-4 (i.e. $\alpha 4\beta 1$) to inhibit inflammatory responses, including asthma, asthmatic lung (see Compositions and Process, columns 24-28). Here, the pharmaceutical compositions are administered in the manner of administration of the particular disease being treated and its severity, including parenteral and local administration such as aerosol in amounts of about 0.25 mg to about 25 mg and about 1 mg/kg/day to about 500 mg/mg/kg/day of the inhibitor peptide, including prophylactically treating patients at risk (see columns 25-28). Arrhenius et al. teach the use of fibronectin and fibronectin derived peptides such as CS-1 and SEQ ID NO: 3 to block various inflammatory conditions by blocking

blocking interactions between the fibronectin peptide CS-1 and VLA-4 (i.e. $\alpha 4\beta 1$) (see entire document, including Background of the Invention, Summary of the Invention and Detailed Description of the Invention).

In addition, Arrhenius et al. disclose Example 5 on treating asthmatic rabbits, which rely upon early phase and late phase allergic reactions (see Example 5 on columns 33-34).

Even though Arrhenius et al. Disclose the costliness of CS-1 polypeptides, the fact that a combination would not be made by businessmen for economic reasons does not mean that a person of ordinary skill in the art would not make the combination because of some technological incompatibility. In re Farrenkopf , 713 F.2d 714, 219 USPQ 1 (Fed. Cir. 1983).

Further, it is noted that in the same paragraph cited by applicant (column 4, paragraph 5), Arrhenius et al. Teach that the role of VLA-4 and the CS-1 peptide in various chronic and acute immunoinflammatory disease states have been established.

In addition, both Wayner et al. and Kogan et al. provide clear direction and motivation to employ the fibronectin polypeptides in the treatment of asthma and allergy at the time the invention was made.

Therefore, Wayner et al., Kogan et al. and Arrhenius et al. all recognized treating both asthma and allergy at the time the invention was made with fibronectin inhibitors.

Given the well known practices of the ordinary artisan in the treatment of asthma, including allergen-induced asthma at the time the invention, which is consistent with the treatment of asthma of fibronectin-derived inhibitors which block the interactions between $\alpha 4\beta 1$ and its receptor between lymphocytes and endothelial cells in order to inhibit inflammatory responses as taught by Wayner et al., Kogan et al. and/or Arrhenius et al. These references are consistent with the acknowledged art in the instant specification as filed that effective dosages of inhibitors are provided in the manner of administration of the particular disease being treated and its severity and the patient's needs, including intravenous and aerosol over a broad range of dosages.

One of ordinary skill in the art at the time the invention was made would have been motivated to select fibronectin-derived peptides, including those comprising EIDLV to treat asthma, including allergen-induced asthma by inhibiting the interaction between lymphocytes and endothelial cells. Given the art known course and treatment of asthma which undergoes acute and chronic phases in responses to allergens, one of ordinary skill in the art would have been motivated to treat asthmatic patients prior to, during and after allergen exposure with the dosages encompassed by the claimed invention. It was routine for the ordinary artisan in asthma would have manipulated the appropriate dosings and modes of administrations to meet the needs of the patients and the course of the disease at the time the invention was made.

The claimed timing of administration and effective dosages were well known in the art, as the ordinary artisan would have applied fibronectin inhibitors to achieve the therapeutic endpoint of diminishing inflammatory conditions in asthmatic patients, including allergen-induced asthmatics. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

Phillip Gambel, PhD.
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Technology Center 1600
February 24, 2003